ROMANTIC LOVE: THE MISTERY OF ITS BIOLOGICAL ROOTS

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Abstract

Love is the most extraordinary human feeling that has inspirated for centuries artists and poets. Only recently it has become a major topic of scientific investigation. The available findings, although limited and scattered, permit to glimpse a fascinating picture regulated by neural mechanisms which have evolved in parallel with the increasing specialization of the human brain. The aim of this paper is to present a comprehensive review of the neurobiological substrates of those complex processes that probably, all together, are part of and/or belong to that feeling which everybody can recognize as love. A particular emphasis will be given to the author's contributions in this area and to some speculative models which may constitute a starting point for deeper investigations of the biological mechanisms underlying love.

The authors' opinion is that a deeper understanding of the biological basis of love should promote the social skills of our species and lead to more rewarding love relationships.

Key words: biological basis of love, love relationships, biological mechanisms underlying love

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Introduction

Romantic love (RL) is a form of bonding which is crucial for the survival of the human species. It can be defined as the establishment of a relationship with a partner (Hazan and Shaver 1987), which is characterized by a specific selection of a him or her, generally amongst individuals outside the family (Marazziti 2002). This is a real paradox: humans are attracted to, courted by and breed with genetically not related individuals whom they would otherwise istinctively avoid. RL can be, therefore, considered the psychological strategy which enables us to overcome neophobia and to mate with and create a strong, often lifelong bond with a complete stranger, so that we may produce healthier offspring. The sum of the emotions+behaviours+subjective awareness of the whole processes constitutes, perhaps, the essence of love.

If some components of these complex processes can be identified also in mammals, what renders RL peculiar and unique is the evidence that the formation of pair bonding in our species is not related only to the reproduction, but also to the creation of group structures, social organizations and interactions with the ultimate goal of providing a safe environment where newborns can be protected until they become autonomous. This is fundamental to the human beings whose offsprings are the weakest and require a longer care than any other mammal.

The nature should have provided mechanisms of increasing complexity for assuring that the focus is limited to one partner only and the sense of safety is formed and maintained, while rewarding the caregivers with that feeling of pleasure and completeness that we call love.

Therefore, it is not surprising that specific brain mechanisms have evolved to accomplish such a goal, that is to say, that RL and love are not regulated by chance, but rather by well-established biological processes for the obvious important consequences of them from the evolutionary point of view.

With no doubt, the evolutionary theories have played a major role in promoting an increasing interest of scientists towards the possible biological bases of love, especially in the past two decades. For a long time, in fact, love, and feelings in general were not been considered worthy enough for becoming a topic of experimental science, had been mainly neglected and surrounded by the scepticism of wasting time and resources in investigating them rather than real disorders (Carter 1998). This was the main obstacle,

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besides the concrete problems for research in this field and, particularly, the subjectivity since scientific methods appeared inappropriate to explore the personal characteristics of emotions that always show peculiarities linked to the particular individual (Porges 1997).

Fortunately the growth of Neuroscience in the past 20 years, has revolutioned the approch to the brain and profoundly mitigated the original scepticism, in that, as LeDoux wrote (2000)" it may also be able to help the resurrection of emotion research by providing a strategy that allows its study independent of subjective emotional experience…"

Therefore, Neuroscience, has ultimately provided reliable tools to explore them. The aim of this paper is to present a comprehensive review of the neurobiological substrates of those complex processes that probably, all together, are part of and/or belong to that feeling which everybody can recognize as love. A particular emphasis will be given to the author's contributions in this area and to some speculative models which may constitute a starting point for deeper investigations of the biological mechanisms underlying love.

Neurobiological correlates of attraction

Attraction represents the starting phase of a RL. It is present in all cultures and societies where it was investigated and, therefore, it is believed to have strong biological roots and to be even genetically transmitted (Jankoviak and Fisher 1992). Most of the times, it is a sudden and unpredictable experience which has the specific aim of favouring the bonding between two not related individuals, since the most distant genetically the parents, the healthiest the second generations. This is supported by some data showing that young girls found more attractive boys who were more different from the genetic point of view (McCoy and Pitino 2002).

According to evolutionary theories, attraction is believed to last between 6 months and 3 years, which is considered the sufficient time that a man might stay close to a woman as long as she becomes pregnant and provides the primary care to the newborn (Fisher 1992).

No biological correlate of the onset of human attraction is available, while different data in animals have highlighted a possible role, in mating selection and subsequent sexual behaviour, of different triggers, such as pheromones, whose role in humans is still debated (Weller 1998, Keverne 2002, Marazziti et al. 2011). Therefore, it seems premature to draw any conclusion on the effects of pheromones on attractiveness and sexual behaviour in humans (Chen and Haviland-Jones 1999, Jacob et al. 2002). Recently, changes of the platelet serotonin transporter, impulsivity traits and even attachment features were observed in a group of women after exposure to male axillary extracts (Marazziti et al. 2010).

We would like to propose a model for attraction which is mainly speculative, although based on what already proposed for basic emotions, such as fear or anxiety: "If we want to understand feelings, it is likely going to be necessary to figure out how the more basic system works...." (LeDoux 2000). We hypothesize that different triggers, such as hormonal changes, life events etc., may change our brain chemistry or functioning, and may, in a certain way, "predispose" our brain to become susceptible to stimuli coming from another individual, and, ultimately, to fall in love (Marazziti and Cassano 2003). The main stimuli would be visual, given the importance of vision for human beings, but also auditory, tactile, gustatory, olfactory. Such stimuli, after the first processing in the thalamus, are generally split into two main bundles: one is directed immediately to the amygdala, through a short pathway, while the other takes a longer way which from the thalamus goes to the cortex and then to the amygdala. The amygdala, when activated, modulates a series of responses in different cerebral areas and peripheral organs; the changes in neurovegetative functions constitute the bases for the subjective feelings of the emotion (Damasio 2003). The cortex, in turn, would be informed by the amygdala itself of its functioning and would discriminate the "quality" (fear? joy? falling in love?) of its activation, so that the individual becomes aware of the feeling. At this point, he or she can easily understand that is in love: this permits a more sophisticated planning of the next appropriate strategies, such as those that enabling him or her to meet again the partner (Marazziti and Cassano 2003). However, the first process is not voluntary and for this reason, it is difficult, although not impossible, to counteract it and, for the same reason, it may not be easily described.

The choice of an individual instead of another would not be casual, because we would choose the one who is able to evoke positive states related to early experiences recorded in our hippocampus, a structure which is anatomically and functionally connected to the amygdala. This is in agreement with psychological constructs that have shown the crucial role of early experiences in the formation of the so-called "love maps" which seem to profoundly affect the choice of the partner. Attraction shows distinctive features. It is generally characterized by an altered mental state with mood elation characterized by sensation of being full of energy and strenght, loss of appetite, sleeplessness, such features resembling the hypomanic phase of a bipolar disorder (Liebowitz 1983, Marazziti and Cassano 2003). Alternatively, attraction may be characterized by mood swings from depression to joy, depending on partner's response, which are again quite similar to the opposite phases of bipolar disorder.

Therefore, it has been suggested that attraction might be underlied by the same neurochemical abnormalities reported in bipolar disorder, such as increased functioning of the norepinephrine and dopamine systems, while a direct role of phenylethylamine, a trace neurotransmitter similar to amphetamines, proposed by Liebowitz 20 years ago, although intriguing, has never been supported by experimental data. Another component of attraction is represented by intense craving of the partner and specific behavioral patterns aiming to evoke a reciprocate response: these patterns are similar to grooming behavior and even to compulsions, so that they might perhaps be due to increased level of dopamine and decreased concentrations of serotonin (Marazziti and Cassano 2003).

Moreover, there occurs also a significant shift of consciousness that is the certainty that our partner is the most extraordinary individual in the world, coupled with a focussed attention on him or her that leads to a decreased interest in routine and mundane activities. This is probably due to increased levels of opioid peptides and dopamine. However, it is generally agreed that the "core" feature of attraction (Fisher 1992) is represented by intrusive thoughts regarding the partner, which resemble obsessions typical of obssessive-compulsive disorder (OCD). Some years ago we demonstrated that OCD and RL share a common dysfunction at the level of the serotonin system (Marazziti et al. 1999). Probably the nature has created this sort of transitory madness in order to render human beings more open and prone towards not related individuals, to be able to overcome neophobia and separation anxiety from original family, and to leave the safe "nest" represented by usual settings. And, really, humans must be "crazy" to forget all their fears when they meet "that special person", to abandon all their reluctance and to show him or her their most intimate aspects.

We, therefore, agree with others (Leckman et al. 1999, O'Dwyer and Marks 2000) that love, pair bonding and pathological conditions, such as OCD and paranoia, can be related to the same neurobiological systems. The risk to become fully "obsessive" or "paranoid" about the partner might be the cost to pay, in evolutionary terms, in order to get a greater likehood of bonding and faithfulness to the relationship. Interestingly, our study showed that the serotonin abnormalities did not last, since, after 12-18 months from the beginning of the relationship, they had returned up to normal values (Marazziti et al. 1999): this is consistent with anthropological studies reporting that attraction lasts no longer that three years (Jankoviak and Fisher 1992).

Consistent with our model that to fall in love is similar to a stressful condition, are the observations that stress and threatening situations may facilitate the onset of new social bonds and intimate ties (Panksepp 1992). The literature relevant to humans in this regard is meagre, albeit in agreement with animal findings, and suggests that the activation of the hypothalamic-pituitary-adrenal (HPA) axis due to stressful experiences may trigger the development of different kinds of social bonding, possibly also that which begins with falling in love (Chiodera et al. 1991). The results of one of our contributions in this field showed that the cortisol levels were higher in subjects in love, as compared with single subjects (Marazziti and Canale 2004). This condition of "hypercortisolemia" was interpreted as a non-specific indicator of some changes which occur during the early phase of a relationship, reflecting the stressful conditions associated with the initiation of a social contact. On the other hand, while LH, estradiol, progesterone, DHEAS and androstenedione levels did not differ between men and women, the testosterone concentrations showed some sex-related peculiarities. In both men and women who were at the early stage of a relationship, they were lower and higher, respectively, than in men and women from the control group. Although none reached pathological levels, all subjects presented this finding, as if falling in love tended to temporarily eliminate some differences between the sexes, or to soften some male features in men and, in parallel, to increase them in women.

The stress related to fall in love may also explain the report of increased concentrations of Nerve Growth Factor, which is a potent antianxiety agent, in romantic lovers (Enzo et al. 2006). The role of neurotrophins (NTS) in RL is supported by our findings that the plasma levels of Brain-Derived Neurotrophic Factor (BDNF) and romantic attachment, are related, albeit differently in the two sexes (Marazziti et al. 2009). In fact, women showed a significant and negative correlation between BDNF levels and the ECR (a self-report questionnaire measuring adult romantic attachment,) avoidance scale, that is to say, the higher the NT concentrations, the lower the avoidance score. This suggests that BDNF may play a role in promoting social relationships through a specific decrease of avoidance and fear of the stranger and unfamiliar individuals. However, it is unclear why BDNF plasma levels and the avoidance of romantic attachment are related only in women, as men of our sample lacked this correlation. It can be hypothesized that the role of BDNF in stress responses might be gender-related, and based on hormonal and genotype interactions. Further studies are, however, necessary to explore whether BDNF, and other NTs, may be related to other human social relationships.

Neurobiological correlates of attachment

If the process of falling in love is successful, that is to say, the partner reciprocates and the two individuals start a RL which continues, after some time from the beginning, the subjective feelings are totally different. The mood is more stable, anxiety is reduced, the mind is free from the obsessive thoughts regarding the partner. Probably, the chemical storm which has flooded the brain like a deluge, has faded away, since it is quite anti-economical and exhausting, because it would involve an extreme release of neurotransmitters and hyperstimulation of receptors that cannot be tolerated too long. Therefore, if the relationship goes on, it is replaced by another process that is represented by attachment (Jankoviak and Fisher 1992, Marazziti and Cassano 2003). Attachment is fundamental for keeping together two individuals, once that the flame of passionate love is vanishing. Romantic attachment could, thus, be defined as the "glue" necessary for tolerating the partner for a long time and for the continuation of a successful relationship.

For a long time, attachment was considered merely as a response to separation, and the biology of attachment was the biology of separation anxiety focusing on opiates (Panksepp 1982). However, nowadays, attachment is believed no longer a consequence of separation anxiety, because it is clear that it includes also another valence linked to the positive feelings and reward related to the formation of social bonds and, as Insel stated (Insel 1997), "... there is no obvious reason for which attachment and separation should be subserved by the same neural system". According to this notion, in the last decade accumulating data have highlighted a key role for

neuropetides such as oxytocin and vasopressin in the initiation and maintainance of infant attachment, maternal behavior and pair bonding (Marazziti et al. 2006, 2008).

A growing body of evidence implicates OT in mediation of complex social behaviours. It may be no coincidence that this peptide has been implicated in prototypically mammalian functions, such as milk ejection during nursing (Wakerley and Lincoln 1973), uterine contraction during labor and in sexual behaviour (Carmichael et al. 1987, Carter 1992).

Oxytocin receptors in the human brain are mainly distributed in the substantia nigra and globus pallidus, areas which have been shown to be activated in adults who were looking at pictures of their partners, or in mothers looking at their children (Bartels and Zeki 2004), together with anterior cingulate and medial insula. This pattern of activation, overlapping with that found during cocaine-induced euphoria (Young et al. 2001, Young 2002), hence supports the notion of a link with the reward pathway (Insel 2003).

Recently, OT administration in humans was shown to increase trust, again supporting the involvement of the amygdala, a central component of the neurocircuitry of fear and social cognition that has been linked to trust and highly expresses OT receptors (Kosfeld et al. 2005).

A recent double-blind study, using functional magnetic resonance imaging to visualize amygdala activation by fear-inducing visual stimuli, showed that human amygdala function is strongly modulated by OT: as compared with placebo, OT potently reduced activation of the amygdala and reduced coupling of the amygdala to brainstem regions implicated in autonomic and behavioral manifestations of fear (Kirsch et al. 2005). It is of interest to note that OT administration did not affect self-report scales of psychological state. This agrees with the observations of Kosfeld et al. (2005), who also did not find an effect of OT on measured calmness and mood and showed that at the level of behaviour, actual social interaction was necessary to bring out the OT effect. Namely, the neural effect of the neuropeptide on behaviour is evident in the social context, but not when subjects rate themselves in isolation. Moreover, the reduction in amygdala activation was more significant for socially relevant stimuli (faces) than for the socially less relevant scenes; differential impairment of amygdala signaling related to the social relevance of the stimuli is in agreement with emerging primate lesion (Prather et al. 2001) and human data indicating that social and non-social fear may depend on dissociable neural systems (Meyer-Lindenberg et al. 2005).

It is interesting to underline that OT seems to be released during different relaxation techniques in humans and, therefore, it is supposed to be one of the mediators of the decrease the stress responses (Carter 1992). Consequently, it has been proposed that it may mediate the benefits of positive relationships in promoting health, such as lower incidence of cardiovascular diseases or depression in individuals with stable partner (Uvnås-Moberg 1998). Along this line, we detected a statistically significant and positive correlation between OT plasma levels and the anxiety scale of the ECR, which showed that the higher the OT levels, the higher the score on the anxiety scale of the ECR (Marazziti et al. 2006). It is not possible to conclude from our data whether the OT levels are a consequence or a cause of the anxiety measured by the scale of the ECR and further research is warranted in order to clarify this. However, in line with the majority of available findings (Carter 1992, Uvnås-Moberg 1997, Insel and Young 2001, Heinrichs et al. 2003), we would suggest tentatively that the former might be the case and that OT might serve to help to counteract anxiety - or at least that form of anxious stress associated with romantic attachment and deep concern over its continuance.

Previously, the relationship between OT and anxiety was sustained only by the indirect evidence that basal OT levels correlate with measures of anxiety, aggression, guilt and suspicion (Uvnås-Moberg et al. 1991) and noise stress provokes the release of the neuropeptide in highly emotional women. Also, other findings have reported that low plasma OT levels would seem to be typical of individuals with low anxiety traits (Turner et al. 2002). Pursuing this line of thought, romantic relationships, and perhaps social relationships in general, could be interpreted as amounting to stress conditions, both acute and chronic depending on the phase (Gillath, et al. 2005). The role of OT would seem generally to be that of keeping anxiety levels under control to a point where they are no longer harmful (in fact, low OT concentrations have been linked with pain syndromes, such as fibromyalgia (Anderberg and Uvnås-Moberg 2000) or abdominal pain (Alfven 2004), but may nevertheless lead to such strategies and behaviours as are best suited to ensuring a partner's continued proximity both during the first stages of the romance and subsequently. Oxytocin might thus be considered an essential element in securing the rewarding effects of a romantic relationship, as a result of its increasing a prospective sexual partner's willingness to accept the risk deriving from social contacts (Kosfeld et al. 2005), through the modulation of anxiety mechanisms. Of course, with particularly vulnerable individuals, if excessively affected by the relationship itself or by other events, these delicate mechanisms might be maladaptive, in the sense that such subjects might become too anxious and thus cross the line between normal and pathological states, even to the point of developing a full-blown psychiatric disorder.

Conclusions

In the present paper, some of the major findings on the neurobiology of RL and love, have been reviewed. This is an emerging and intriguing field of research which only recently has become the topic of intensive scientific investigations and has received benefits from the application of the most advanced methods provided by Neuroscience. The scattered data which have been gathered and are accumulating at an increasing amount, permit to set up an initial framework and hypotheses that await to be tested. Love still remains a great, albeit fascinating, mistery that Neuroscience begins to uncover. We think that the understanding of its biological roots will never diminish the sense of wonder and happiness that fulfills us when we love and are loved, rather, it

will increase our potentiality to love better and promote our social relationships.

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